Supplemental figure and table legends

Figure S1. A) Axial CT images of the right and left temporal bones of a 40-45 year old female, the mother of DGAP353. While the inferior basal turns appeared normal (not shown), the upper basal and middle turns of each cochlea appear flattened (wide arrow in image 1). The round windows appear mildly narrow. The right cochlear aperture (short line in image 3) measured 1.5 mm TR and the left measured 1.3 mm TR. There is variant anatomy of the internal auditory canals which appear mildly flared on axial images at the level of the porus acusticus, however normal in the coronal plane. The sinus tympani (posteromedial recess of the tympanic cavity) is unusually small bilaterally (short arrow in image 3). B) Reformatted coronal CT images of the right and left temporal bones of the mother of DGAP353. The right oval window is mildly narrow in height (long arrow in image 1). The round window is also narrowed (short arrow in image 2). Note the mildly small upper cochlear turns (arrowhead in image 3). The left oval window is also mildly narrowed and opacified. The inferior osseous margin of the tympanic segment of the facial nerve

canal is not clearly seen, raising concern for dehiscence at the level of the stenotic oval window (arrow in image 4). The subjacent round window appears normal in the coronal plane. C) Axial CT images of the temporal bones of a 10-14 year old female, DGAP353. Imaging reveals normal upper cochlear turns. The cochlear aperture measures 1.6 mm on each side. The sinus tympani is unusually small bilaterally (short arrows). Note the normal right stapedial crura (long arrow in image 1). The left stapedial crura are closely approximated and indistinct (long arrow in image 2). D) Reformatted coronal images of the temporal bones of DGAP353. These images reveal that the left oval window (arrow in image 1) and round window (arrow in image 2) are stenotic. The right sided oval and round windows were also slightly narrow (not shown).

Figure S2. A) Chromosome diagrams depict the translocation between Xp11.4 and 11q24.2 in DGAP148. Above, TADs containing the breakpoints are shown, with the breakpoint positions indicated by vertical yellow bars. Protein-coding genes are shown in blue and non-coding genes in green, with a single isoform depicted per gene. TAD borders were defined in (Dixon et al. 2012). Triangular contact maps display micro-C data from (Krietenstein et al. 2020). B) Expanded view of the genomic region surrounding the 11q24.2 breakpoints in DGAP148. The directly disrupted lncRNA *ENSG00000255087* is highlighted in red. C) Expression of the lncRNA *ENSG00000255087* from the GTEx database (Lonsdale et al. 2013).

Figure S3. A) Expanded view of the genomic region surrounding the Xp11.4 breakpoints in DGAP148. B) Expression of the protein-coding gene *KIRREL3* from the GTEx database (Lonsdale et al. 2013).

Figure S4. A) Chromosome diagrams depict the translocation between 3q26.33 and 9q21.13 in DGAP355. Above, TADs containing the breakpoints are shown, with the breakpoint positions indicated by vertical yellow bars. Protein-coding genes are shown in blue and non-coding genes

in green, with a single isoform depicted per gene. TAD borders were defined in (Dixon et al. 2012). Triangular contact maps display micro-C data from (Krietenstein et al. 2020). B) Expanded view of the genomic region surrounding the 3q26.33 breakpoints in DGAP355. The directly disrupted lncRNA *SOX2-OT* is highlighted in red. C) Expression of the lncRNA *SOX2-OT* from the GTEx database (Lonsdale et al. 2013).

Figure S5. A) Expanded view of the genomic region surrounding the 9q21.13 breakpoints in DGAP355. B) Expression of the protein-coding gene *SOX2* from the GTEx database (Lonsdale et al. 2013).

Table S1. Genetic and phenotypic details for all cases analyzed as part of this study. Genomic coordinates refer to GRCh38/hg38. Derivative A and Derivative B represent the chromosomal breakpoints listed in the order recommended by Orulu et al. 2014.

Table S2. Details regarding the breakpoints and the directly disrupted genes for all 66 cases in which we identified a disrupted lncRNA. The first tab lists cases in which only lncRNAs are directly disrupted. The second tab lists cases in which lncRNAs are directly disrupted along with other genes. Genomic coordinates refer to GRCh38/hg38. The disruption of the lncRNA *RMST* in DGAP032 was previously reported in (Stamou et al. 2020). The disruption of the lncRNA *LINC00299* in DGAP162 was previously reported in (Talkowski et al. 2012a).

Table S3. Additional details for the cases in which only lncRNAs were directly disrupted. The first tab lists the nearest protein-coding gene to each disrupted lncRNA. The second tab lists all genes of any class within 100kb of the breakpoints, excluding the lncRNAs that are directly disrupted (see Table S2 for directly disrupted lncRNAs). Genomic coordinates refer to GRCh38/hg38.